AMENDMENTS

In the Specification:

Please replace the paragraph beginning at page 31, line 17, with the following amended paragraph.

A construct of rad3, in which the 794 amino acids between aa 1477 and aa 2271 (including kinase domain) were replaced with a ura4+ gene, was created using the methodology describerd in Barbet et al. (1992). A linear fragment of this was used to transform sp011 to uracil prototropy and single copy integration at the rad3 locus was checked by Southern blotting. To create the site specific kinase null mutations, a C-terminsl 3.01 kb bamHI-salI fragment of rad3 was mutated with either (A: GTTTTCGCCATGGCGCGCTCCCAAACCCAA (SEQ ID NO: 5), B: TTCATCAAACAATATCTTTTCGCCATGGCG (SEQ ID NO: 6), or C: CAAAAAGACAGTTGAATTCGACATGGATAG (SEQ ID NO: 7) in order to introduce either the D2230A, N2235K or D2249E mutations into the kinase domain. Analgous changes have previously been used in the analysis of P13 kinase vps34 of S. cerevisiae (Schu et al. 1993). These fragments were then used to transform the rad3.d null mutant and gene replacements selected by their ability to grow on FOA containing media (Grimm et al. 1988). All strains were checked by Southern blotting. Full length expression constructs of rad3.D2230A were created in pREP1 and pREP41 (Maundrell, 1990) by standard subcloning following introduction of an NdeI site at the ATG and deletion of three internal NdeI sites.

Please replace the paragraph beginning at page 32, line 6, with the following amended paragraph.

To isolate an appropriate probe for identifying cDNAs corresponding to a human rad3 homologue, degenerate oligonucleotides were designed against the amino acids LGLGDRH (5' oligo; oDH18)(SEQ ID NO: 13) and HVDF[D/N]C (3' oligo; oDH-16)(SEQ ID NO: 14) or Rad3/Esr1p. Inosine was incorporated at positions of four-fold degeneracy, and primers were tailed with BamHI (oDH18) and EcoRI (oDH16) to facilitate cloning. DNA sequencen analysis of the ~100 bp PCR product obtained from amplification of peripheral blood leukocyte cDNA demonstrated significant similarity to MEC1/rad3. This sequence was used to synthesize a non-degenerate primer (oDH-23;

GACGCAGAATTCACCAGTCAAAGAATCAAAGAG (SEQ ID NO: 8) for PCR with an additional degenerate primer (oDH17) designed against the amino acid sequence KFPP[I/V][L/F]Y[Q/E]WF (SEQ ID NO: 12) of Rad3/Esr1p. The 174 bp product of this reaction was used directly to screen a macrophage cDNA library. Four positive clones were isolated (the largest approximately 3 kb).

Please replace the paragraph beginning at page 33, line 8, with the following amended paragraph.

Northern blot hybridisation: a 1.3 kb PCR product was amplified in the presence of ³²P-dCTP using primers 279-3 (TGGATGATGA CAGCTGTGTC (SEQ ID NO:9)) and 279-6 (TGTAGTCGCT GCTCAATGTC (SEQ ID NO:10)). A nylon mambrane containing 2µg of size-fractionated poly A+ RNA from a variety of human tissue sources (Clontech Laboratories) was probed as recommended by the manufacturer except that the final wash was performed at 55°C rather than 50°C to minimize the possibility of cross-hybridization to related sequences.

Please replace the paragraph beginning at page 33, line 16, with the following amended paragraph.

We mapped the ATR gene to chromosome 3 by a combination of fluorescent in situ hybridisation and polymerase chain reaction (PCR) based assays. FISH analysis using a cDNA clone identified the ATR gene on chromosome 3. Two primers (oATR23: GACGCAGAATTCACCAGTCAAAGAATCAAAGAG (SEQ ID NO: 8) and oATR26: TGGTTTCTGAGAACATTCCCTGA (SEQ ID NO: 11)) which amplify a 257 bp fragment of the ATR gene were used on DNA derived from human/rodent somatic cell hybrids containing various human chromosome panels available from the NIGMS Human Genetic Mutant Cell Repository (Drwinga *et al.* 1993). PCR with the same primers was used to sub-localise ATR to a specific region on chromosome 3. The templates for these amplifications consisted of DNA samples from patients with truncations along chromosome 3 (Leach *et al.* 1994).